Assessment of Vestibular System Function

[1]Dalia Helal Galhom, [1]Rana Mohamed Talaat, [2]Diana Hanna, [1]Nahla Hassan Gad,
[1]Audio-Vestibular Medicine, ENT Department, Faculty of Medicine, Zagazig University, Egypt
[2]Pediatrics Department, Faculty of Medicine, Zagazig University, Egypt
Corresponding author: Rana Mohamed Talaat
Email: rotatota93@gmail.com, **Mobile:** 01002184602

Abstract

Life-long transfusion therapy with ironchelators is a treatment choice for patients with beta-thalassemia major. Some investigators have proposed vestibular impairment related to the use of deferoxamine, so vestibular system function assessment is important.

KeyWords:Vestibular, cVEMP, VNG.

DOINUMBER:10.48047/NQ.2022.20.19.NQ99420 **NEUROQUANTOLOGY2022;20(19):4568-4575**

Introduction.

Many tests are done to evaluate vestibular system function; the results enable for a reliable identification of the reason. Videonystagmography (VNG) is an important tool in the diagnosis of dizziness because it distinguishes between the central and peripheral vestibular systems **(1).**

Furthermore, cervical vestibular evoked myogenic potentials (cVEMP) and ocular vestibular evoked myogenic potentials (oVEMP) are vestibular tests capable of evaluating the otolith organs, thus investigating utricular and saccular functions and, indirectly, differentiating superior and inferior nerve involvement. As a result, observing indirect and latent vestibular system impairments in asymptomatic individuals also may be beneficial **(2).**

➢ Videonystagmography (VNG):

VNG is a complete diagnostic system for recording, analyzing, and reporting eye movements using video imaging technology, in which hi-tech video goggles with infrared cameras are used. VNG includes a series of tests used to determine whether a vestibular disease may cause a balance or dizziness problem**(1).**

VNG helps document unilateral/bilateral loss of vestibular function and detect central lesions that are missed during a routine physical exam. VNG helps decide whether additional tests (e.g., MRI) are needed and helps in preoperative evaluation – for example, of acoustic neuroma. The VNG pretest protocol includes patient interview, otoscopic ear examination, eye movement examination to modify camera configuration, and finally placement of goggles and calibration of eye movement**(2).**

V.N.G tests includes the following:

- Tests of oculomotor function (with fixation): includes saccade, tracking, and optokinetic tests.
- Tests of gaze stabilization (with or without fixation, alertness level): includes gaze/spontaneous nystagmus.
- Tests for specific etiologies includes Dix–Hallpikemaneuver (dynamic positioning), positional tests and Caloric test **(1).**

(A) Oculo-motor tests:

Just as the eye serve as window for investigating the function of the peripheral vestibular system, they also provide a mean to investigate the oculo-motor pathways in the brainstem and cerebellum that are required for the function of the VOR. There are a variety of testing paradigms that can assist in identifying abnormalities in the central oculo-motor control systems **(3).**

1. Saccade test:

This test assesses the ability to rapidly move the eye and refixate on the target, and appraises the latency, accuracy, and velocity of the saccade **(3).**

Abnormal saccades:

- ***Saccadic slowing*** denotes the presence of a central lesion in the basal ganglia, brain stem, cerebellum, peripheral oculomotor nerves, or muscles (typically in diffuse lesions of the central pathways associated with neurodegenerative diseases). It can also be due to fatigue, drowsiness, or medication (reversible)**(4).**
- ***Delayed saccades*** (latencies>>200 ms): These denote a central lesion in the frontal/frontoparietal cortex or basal ganglia (interpreted conservatively). This condition has low clinical value if bilateral (more significant if unilateral)and may be caused by inattention, poor visual acuity, or medications**(3).**
- ***Saccadic dysmetria***: Hypometria denotes a central lesion in the cerebellar flocculus while hypermetria denotes a central lesion in the cerebellar vermis**(3).**

2. Smooth pursuit test:

Tracking is the ability to smooth pursuit, which is controlled by the vestibuleocerebellum**(4).** Unilateral defective tracking (pursuit) denotes the presence of a central lesion. A symmetric defect indicates the presence of diffuse cortical, basal ganglial, or cerebellar anomalies. An asymmetric defect indicates the presence of focal lesions involving the ipsilateral cerebellar hemisphere, brain stem, or parieto-occipital region. Bilateral defective pursuit (stair step appearance or cogwheel) mostly occur with multiple sclerosis **(1).**

3. Optokinetic test:

The optokinetic system is responsible for the stabilization of the visual field. VNG tests the optokinetic tracking of targets by passing a light rapidly in front of a patient from one direction to the other. Asymmetries are noted and are signs of central nervous system dysfunction **(2).**

4. Gaze evoked nystagmus:

The ability to maintain eccentric gaze is under control of the brainstem and midline cerebellum, particularly the vestibulocerebellum (especially the flocculonodular lobes). When these mechanisms fail to hold the eye in the eccentric position, the eye drifts toward the midline (exponentially decreasing velocity), followed by refixation saccades toward the target. Such gaze-evoked nystagmus is central in origin and always beats in the direction of intended gaze. Causes of gaze-evoked nystagmus include a drug effect (sedatives, antiepileptics), alcohol, CNS tumors, and cerebellar degenerative syndromes **(5).**

(B) Spontaneous nystagmus:

Spontaneous nystagmus occurs because of loss of tonic input from affected labyrinth. Peripheral nystagmus may have a torsional component which can make it look slightly vertical. Nystagmus from a peripheral lesion can decrease or stop if patients are asked to fixate their eyes on a target. Vertical nystagmus is always due to a central cause since those signals, compared to peripheral, run through a different tract to third nerve nucleus **(6).**

(C) Tests for specific etiologies: includes Dix–Hallpikemaneuver (dynamic positioning):

It is the classic maneuver described to detect a posterior canal BPPV. It causes nystagmus with the head hanging down or when switching to upright position from lying down. This test is specific for posterior canal BPPV which precipitates the nystagmus and dizziness. A more useful approach which is suggested and the readers can verify is a "vestibular shake-up using Dix-Hallpike type maneuver" with a rapid, forceful elevation aimed at shaking up the whole vestibular system. The rapid forceful movement of the neck precipitates the typical dizziness in most patients, even if there is no nystagmus **(7).**

(D) Positional tests:

The more common positions include: sitting head turned right, sitting head turned left, supine head turned left, supine head turned right, right decubitus, left decubitus, and pre-irrigation position (head and shoulder elevated by 30 degree up from the horizontal plane). In cases where no cervical region injuries or active pathologies are reported ,use of head hanging straight, right and left adds three additional positions for testing prior to the pre-irrigation position. The purpose of this subtest is to investigate the effect of different head positions within the gravitational field. Positional nystagmus is typically classified by the direction of the fast component of the nystagmus but measured by the velocity of slow component **(4).**

(E) Bithermal Caloric Testing:

Bithermal caloric test is often used to test the horizontal canal function. Temperature fluctuations can induce endolymph shifts causing hair cell activation. Typically, each ear is irrigated with water at 30°C and 44°C with eyes open behind Frenzel lenses.Traditional VNG testing only evaluates superior branch of the vestibular nerve and angular vestibuloocular reflex pathway (8).

Unilateral weakness (canal paresis): It denotes a peripheral vestibular lesion involving the lateral (horizontal) canal or its afferent pathways on the side of the weaker response (involved pathway extends from the end organ to the root entry zone of the vestibular nerve in the brain stem). In the acute phase, significant spontaneous nystagmus is present (2).

It can be caused by diseases that affect the labyrinth, the vestibular nerve, or the blood supply to these sites. Central lesions that affect the root entry zone of the vestibular nerve (e.g., multiple sclerosis) can cause unilateral weakness but other central nervous system signs may also be present(4).

Bilateral weakness (BW): When bilateral caloric weakness is present, an additional test (rotation chair, active head rotation, head thrust, or bilateral ice water tests) is needed to determine whether true bilateral vestibular lesion or hyporesponsiveness exists. Hyporesponsiveness (BW) denotes either peripheral vestibular lesion in both ears or a central lesion (1).

- Vestibular evoked myogenic potentials:

Vestibular evoked myogenic potentials (VEMPs) are short-latency, vestibular-dependent reflexes that are recorded from the sternocleidomastoid (SCM) muscles in the anterior neck (cervical VEMPs) or (cVEMPs) and also recorded from inferior oblique (IO) extraocular muscles (ocular VEMPs) or (oVEMPs). They are evoked by short bursts of sound delivered through headphones or vibration applied to the skull. As these stimuli have been shown to preferentially activate the otolith organs rather than the semicircular canals, VEMPs are used clinically as measures of otolith function(9). VEMPs have become a standard component of the neuro-otology test battery over the past 20 years (10).

Cervical vestibular evoked myogenic potential (cVEMP):

Cervical VEMPs were first described by Colebatch and colleagues, who reported a click-evoked muscle reflex in the ipsilateral SCM, which was dependent upon vestibular, but not auditory function (9). The stimulatiom of SCM muscle activity could be easily produced using standard evoked potential equipment and calibrated headphones. Intramuscular recordings later confirmed that the surface response is produced by a short inhibition of the SCM muscle(11).

The cVEMP tracing consists of a positive peak at approximately 13 ms and a negative peak at approximately 23 ms and represents the saccule's response to sound when using an air-conducted stimulus (Figure 1). To elicit the air-conducted cVEMP response, the stimulus must be a brief click or a low frequency (e.g. 500 Hz) tone burst. The 500 Hz tone burst has been shown to best stimulate the saccule (11).

Both otolith organs (i.e. the saccule and the utricle) are activated when stimulated via bone conduction (12). Based on robustness of amplitude and Sternocleidomastoid activity (SCM), cVEMP testing is most successful when the patient lies supine with head elevated and turned away from the stimulated ear (13).

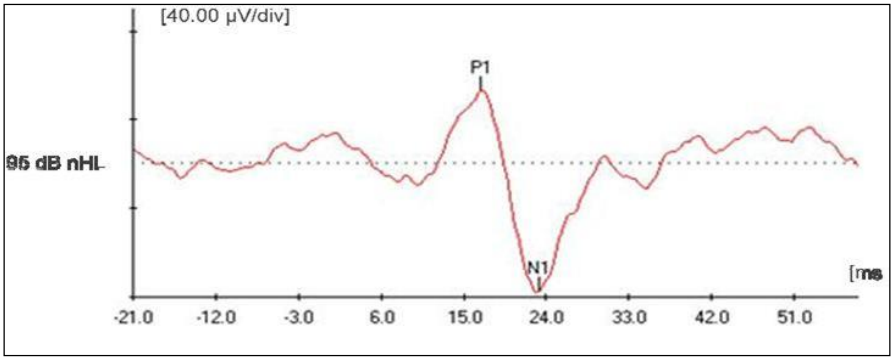

Figure (1): Wave form of cVEMP(14).

Neural Pathways of cVEMP:

P13 and N23 cVEMP waveform is a myogenic potential arising from the vestibulocollic reflex (VCR) of the vestibulospinal tract, which is used to maintain head and neck stability. The cVEMPis evoked in response to sound and originates from the vestibular system, most likely the saccule. A later response(N34, P44) is independent of the vestibular system and most likely arises from the cochlea (12).

The VCR arc includes the receptor (the saccule), the afferent pathway (the inferior vestibular nerve), and the efferent pathway (the lateral vestibulospinal tract, the medial vestibulospinal tract, and the end muscle (Figure 2) (9).

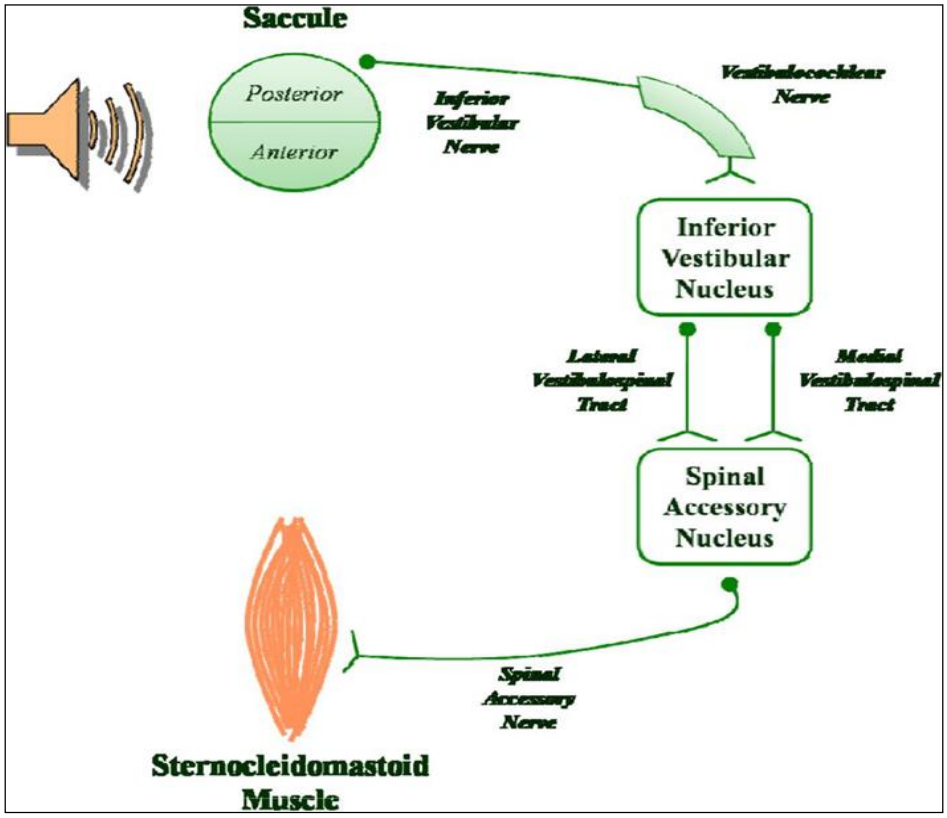

Figure (2): Diagram of the cVEMP neural pathway evoked by an air-conducted stimulus (15).

Stimulus and recording parameters:

Air conducted (AC) sound is the most common VEMP stimulus modality. Clicks (0.1 ms square waves) were used in the initial report on cVEMPs and remain good stimuli, as they have a very fast onset and stimulate across a range of frequencies (approx. 1–4 kHz)(16).

Tone burst-evoked VEMP responses had lower stimulus thresholds, larger amplitude than click-evoked ones. Tone burst stimulation at 500Hz tone was considered as an ideal stimulation, with the stimulus intensity that ranged between 95–105dBnHL. Tone burst stimulation at 95dBnHL was the most commonly used (17).

Transmission to the saccule shows frequency tuning, with preferred frequency at approximately 500–1000 Hz, and therefore AC tone bursts around these frequencies are also good stimuli. There are, however, mean differences in tuning with age and between cVEMPs and oVEMPs, whereby higher frequencies produce larger reflexes in older subjects and for oVEMPs(10).

Frequency tuning can also change in some inner ear diseases, such as Meniere's Disease (MD), whereby patients have larger responses to 1 kHz than 500 Hz stimulation, and superior semicircular canal dehiscence (SCD), in which patients have broader tuning (9).

Clicks are typically delivered with 0.1 ms duration, though can be longer. Likewise, tone bursts can be several milliseconds in duration. Increasing stimulus duration typically increases VEMP amplitude, as the total sound energy delivered to the inner ear isincreased. However, the enhancement with increasing duration reverses after approx. 6–8 ms for cVEMPs and earlier for oVEMPs(18).

Rise time has a significant effect on the size and latency of the VEMP. The otolith organs may be sensitive to changes in acceleration over time and thus VEMPs are larger and peak earlier if the onset of a stimulus (i.e., rise time) is short. In fact, stimulus rise time is one of the major factors determining reflex latency and for this reason it is important to collect normal data for each stimulus(9).

The optimal AC VEMP stimulus intensity is close to the upper limit of safe sound exposure for the cochlea. This is necessary as in normal humans the average threshold for a VEMP is around 114 dB pkSPL and this increases with age. Although the vestibular and auditory sensory organs are housed together within the bony labyrinth, the vestibular system is normally shielded from environmental sound, which is very efficiently directed to the cochlea(16).

Ocular Vestibular Evoked Myogenic Potential (oVEMP):

Ocular VEMPs were first described a decade after the cVEMP. They are evoked by the same stimuli but are reflexes of the extraocular muscles and thus represent activation of the vestibulo-ocular reflex instead of the vestibulo-collic reflex. The oVEMP originates in the inferior oblique muscle and is produced by a brief excitation of the muscle (12).

Only very loud sounds are sufficiently intense to activate the otolith hair cells. As such, there is only a relatively small intensitywindow for stimulating the vestibular system with AC sound: between the vestibular acoustic threshold and the upper limit of safe stimulation. Careful calibration of stimuli is therefore critical (19).

Electrode montage:

cVEMPs should be recorded using surface electromyography (EMG) electrodes with an active (noninverting) electrode placed on the upper third to midpoint of the SCM muscle(the patient is asked to activate the SCM), and a reference (inverting) electrode placed on or near the sternum. The common or ground electrode can be placed on the forehead(10).

Monaural stimulation is preferable to binaural stimulation for both reflexes to ensure that only responses from one ear or muscle are recorded during each trial. The cVEMP is usually only present in the ipsilateral SCM, however the reflex is not strictly unilateral. Stimulation of one ear can sometimes produce an inverted 'crossed response' in the contralateral SCM (18).

VEMP parameters generally used for interpretation were the presence or absence of a VEMP response, VEMP threshold, latency of P13 and N23, and P13-N23interamplitude. Other VEMP parameters including P13-N23interlatency, interaural difference of P13 and N23 latency, and interaural amplitude difference (IAD) ratio (20).

Evidence suggests that the oVEMPis produced by otolith afferents in the superior vestibular nerve (which contains all utricular afferents and a small number of afferents from the anterior saccule). Given this, and the fact that sacculo-ocular pathways are thought to be weak, the oVEMP is considered a test of utricular function (12).

The discovery of the oVEMP response and its neuronal pathway encouraged researchers to explore the procedure's stimulation and recording methods.

Todd et al., (21) demonstrated a short latency vestibular evoked potential with a negative peak at 10 ms (N10) and a positive peak around 15 ms in response to a loud 500 Hz air-conducted stimulus (Figure 3).

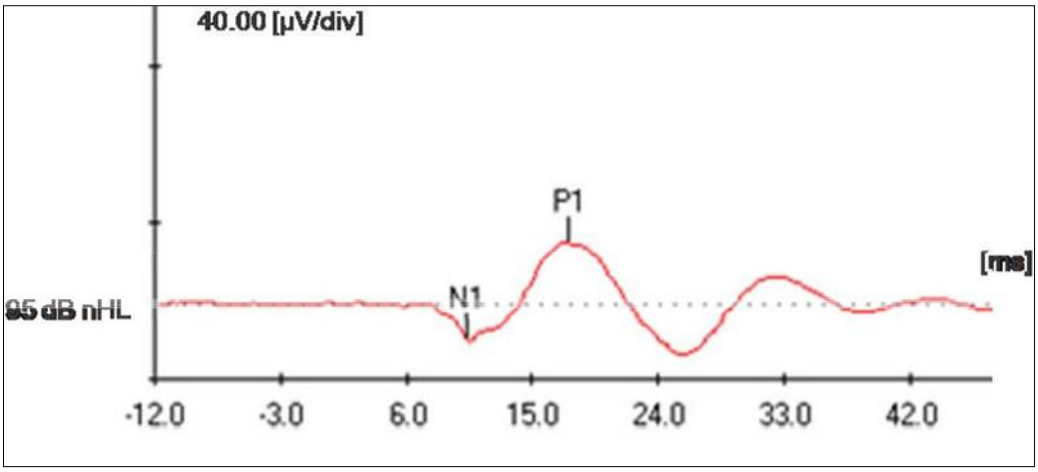

Figure (3): Ocular VEMP response **(22).**

Neural pathway of oVEMP:

The neuronal pathway for oVEMP via the vestibulo-ocular reflex including activation of the vestibular nerve and vestibular nuclear complex traveling up the medial longitudinal fasciculus(where at some point it decussates ending at the oculomotor nuclei), then to ocular nerves and the extraocular muscles (Figure 4)**(23).**

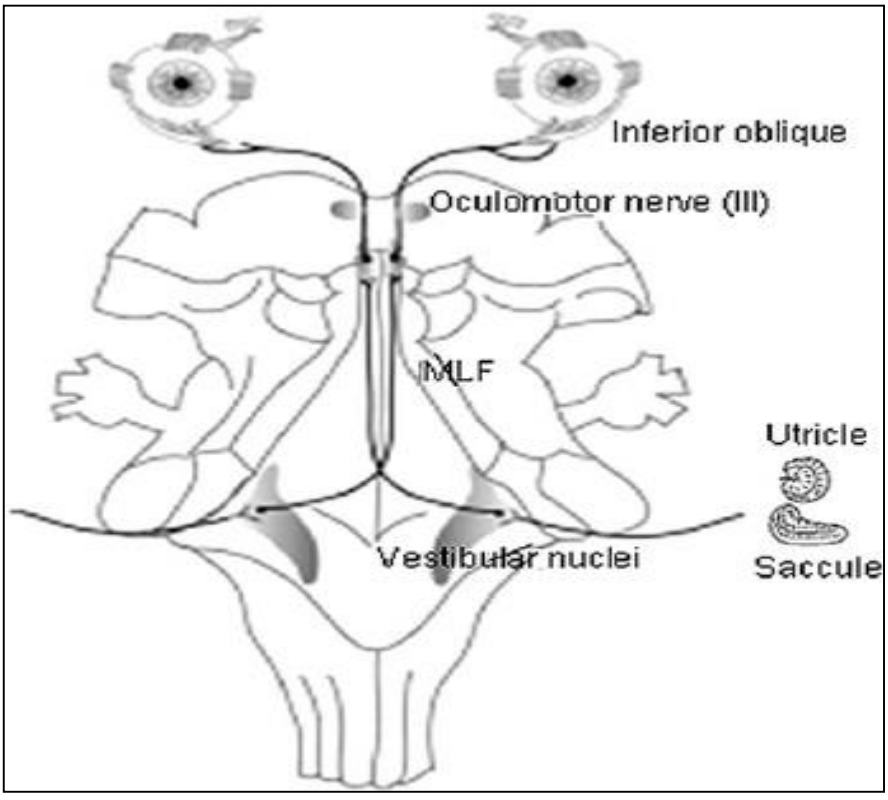

Figure (4): Neural pathway of oVEMP (**23**).

Stimulus parameters:

As the oVEMP pathway is being confirmed, researchers are simultaneously studying oVEMP findings. Various stimulation methods elicit the oVEMP response: air conduction, bone conduction, forehead tap and galvanic stimulation, though air and bone conduction stimulation are the most studied. When using an air-conducted stimulus, a 500 Hz tone burst is more effective in producing optimal results than when using a click stimulus **(18)**.

oVEMPs have similar parameters as well as cVEMPs, but the response is recorded from the contralateral eye of the stimulated ear. Air and bone conduction oVEMP responses are shown to have similar tuning frequencies (i.e. 500 Hz tone burst) as cVEMP responses **(10).** Air conduction oVEMPcan be obtained through a monaural or binaural stimulus presentation with similar results **(9**).

Electrode montage:

Like the cVEMP, oVEMPs scale with stimulus intensity and muscle contraction are recorded with surface electrodes placed on the cheeks underneath the eyes(active electrode) while the patient looks upwards, the negative electrode about 1 cm below the active one on the cheek, and the ground electrode on the forehead. In contrast to the cVEMP, the oVEMP is a contralateral reflex, recorded from the eye opposite the stimulated ear. oVEMPs are used clinically to assess the function of the utricle **(11).**

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*e*ISSN1303-5150

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*e*ISSN1303-5150